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Prevalence and mortality among patients with COPD hospitalised by ambulance in the 2007-2018 period

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ABSTRACT

INTRODUCTION. Severe exacerbations in chronic obstructive pulmonary disease (COPD) may require acute medical attention by calling the emergency medical services (EMS) for an ambulance. The 30-day mortality for EMS patients with respiratory diseases appears to have stagnated, which may be due to changes in age, comorbidity or disease severity. We examined trends of occurrence, severity and mortality for EMS patients with COPD.

METHODS. A historical population-based cohort study was conducted encompassing patients with COPD who requested an ambulance in the North Denmark Region in the 2007-2018 period. We described acute severity by oxygen saturation and respiratory rate at the arrival of the ambulance along with comorbidity and duration of hospitalisation.

RESULTS. A total of 5,969 EMS patients with COPD were identified and the figure nearly doubled from 2007 to 2018. Age and comorbidity were higher in the last part of the period. Furthermore, the initial respiratory rate was higher, oxygen saturation was lower and the duration of hospitalisation was lower in the last part of the period. The 30-day mortality rose from 12.6% to 15.4%, but the odds ratio was not statistically higher and decreased after adjustment.

CONCLUSIONS. COPD constituted increasing proportions of those admitted to hospital after calling the EMS. The mortality among EMS patients with COPD may be due to patients being older, having more comorbidities or being more severely acutely ill. The mortality suggests that COPD patients requesting an ambulance should be considered severely ill.

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Severe exacerbations in chronic obstructive pulmonary disease (COPD) may require acute medical attention and hospitalisation [1]. For some patients, the emergency medical services (EMS) are called to request an ambulance due to the acute severity of their condition. At the arrival of the ambulance, respiratory rate and oxygen saturation are measured and treatment is initiated.

Patients with acute respiratory illness constitute a large proportion of all patients calling the EMS [2], also among Danish patients calling the EMS for an ambulance [3, 4]. In the North Denmark Region, we previously found that the 30-day mortality among patients calling the EMS in the 2007-2014 period due to circulatory diseases

decreased from 20% to 12% in the course of the period. However, the 30-day mortality due to respiratory diseases remained unchanged at 11-12% in the same period [4]. The most frequent diagnosis among adult patients calling the EMS in the North Denmark Region in 2012-2015 was COPD [5]. The ageing Danish population may lead to an increased number of COPD cases and this may contribute to a high mortality due to respiratory diseases.

Our aim was to investigate trends in prevalence, duration of hospitalisation and mortality among patients suffering from COPD who requested an ambulance in the course of a decade, and to examine whether differences in age, comorbidity and acute severity at ambulance arrival may explain the trends observed.

METHODS

This was a historical population-based cohort study of patients with COPD who requested an ambulance in the North Denmark Region in the 2007-2018 period.

The North Denmark Region, one of Denmark's five administrative health care regions, has 587,000 inhabitants and three hospitals with emergency departments.

An ambulance may be requested by calling the national emergency number or by request from a general practitioner. A nationwide electronic prehospital medical record was implemented in all ambulances in 2015 (used since 2006 in the North Denmark Region). The prehospital medical record stores observations noted by the ambulance personnel and vital signs recorded directly from a transportable monitor [6]. The unique Danish civil registration number made linkage between registries and medical records possible.

Patients brought to a hospital are diagnosed at discharge according to the International Statistical Classification of Diseases and Related Health Problems, 10th Revision (ICD-10) [7].

Participants

We included patients brought to a hospital by ambulance following an emergency call who were subsequently diagnosed with COPD as their main hospital diagnosis in the North Denmark Region in the 2007-2014 and 2016-2018 periods. Due to the introduction of a nationwide version of the prehospital medical record system during 2015, we excluded this year. We excluded patients who did not reside in the North Denmark Region during the 30 days following the emergency call. As it is not possible to identify a hospital contact for patients without a civil registration number, patients without a civil registration number were excluded from the study population.

Data sources and variables

Ambulance data were retrieved from the logistic systems EVA 2000 and Logis CAD. Respiratory rate and oxygen saturation were obtained from the electronic prehospital medical record (Amphi Systems A/S, Aalborg, Denmark). Diagnoses, date of admission and discharge were extracted from the regional Patient Administrative System. Date of death was obtained from the Danish Civil Registration System [8].

We defined COPD according to the specific ICD-10 main diagnoses (https://ugeskriftet.dk/files/a06210526_supplementary.pdf **Table 1**). We chose this approach as the main diagnoses describe the condition upon which hospital physicians act.

The first registered respiratory rate and oxygen saturation at the arrival of the ambulance were used to assess the acute respiratory condition [9]. We excluded values above 100% for oxygen saturation and above 100 breaths per minute for respiratory rate. Comorbidity was described using the Charlson Comorbidity Index (CCI) based on hospital diagnoses, including COPD and asthma, in the five years leading up to the call for an ambulance. The

CCI is a combined score of previous medical conditions. A CCI score of 0 corresponds to no comorbidity, 1-2 to mild, 3-4 to moderate and 5 or above to severe conditions [10]. The COPD diagnosis given at the current hospitalisation was not included in the CCI score. We defined 30-day mortality as death within 30 days after the ambulance contact.

Statistical analysis

Analyses were stratified into three periods (2007-2010, 2011-2014 and 2016-2018) to achieve more robust estimates than year-to-year analyses would have produced. Trends in frequency and the prevalence proportion (compared with the size of the population in the North Denmark Region obtained from Statistics Denmark), age, comorbidity, oxygen saturation, respiratory rate and duration of hospitalisation during the three periods were analysed using nonparametric tests for trend (the Jonckheere-Terpstra test). Associations between ratio-interval measures were analysed by Kendall's rank correlation due to the screwed distribution of the measures. We defined statistical significance at the 5% level. Patients requesting an ambulance more than once in the study period were included in the analyses with each episode except for the mortality analyses, which were based on the patients' latest contact. The Kaplan-Meier survival curve was used to describe mortality. Logistic regression was used to estimate odds ratio (OR) and 95% confidence intervals (CI) for 30-day mortality using the 2007-2010 period as reference and adjusting for age and comorbidities to account for an ageing population and adjusting for oxygen saturation and respiratory rate to account for the acute severity of the condition. A possible linear trend in the change of OR across the three periods was evaluated using post-estimation contrasts. STATA version 16.0 (STATA Corporation, College Station, USA) was used for the analyses.

Ethics

The project is registered with the North Denmark Region (project ID number 2016-80). Furthermore, The Danish Patient Safety Authority approved the handover of prehospital medical record data required for the study (3-3013-1675/3).

Data sharing statement

The study included sensitive patient information; restrictions therefore apply, and data are not publicly available. However, researchers with an interest in the topic can seek approval from the Danish Patient Safety Authority. Once approval has been obtained, data can be requested from the Centre for Prehospital and Emergency Care, Aalborg, Denmark.

Trial registration: not relevant.

RESULTS

In the study period, 283,764 patients called the emergency number requesting an ambulance, and 230,797 were brought to a hospital. Among these, 5,969 patients were diagnosed with COPD at discharge. A total of 60% (2,622) requested an ambulance more than once in the study period; 18% twice, 9% three times, 7% four times and 27% more than five times.

During the study period, the number of patients doubled, from 324 in 2007 to 655 in 2018; the prevalence proportion therefore rose from 5.6/10,000 inhabitants to 11.1/10,000 inhabitants (https://ugeskriftet.dk/files/a06210526_supplementary.pdf - **Table 2**). As the overall number of ambulance missions also increased in the study period, patients diagnosed with COPD constituted from 324 (1.7%) in 2007 to 655 (2.0%) ($p < 0.001$) in 2018. (https://ugeskriftet.dk/files/a06210526_supplementary.pdf - **Table 2).**

Across the three periods, the age of the patients increased from a median of 70 years to 74 years (**Table 1**).

TABLE 1 COPD patients transported to hospital by ambulance in the North Denmark Region 2007-2014 and 2016-2018, divided into three periods.

	2007-2010	2011-2014	2016-2018
n	1,585	2,393	1,991
Age, median (IQR), yrs	70.4 (62.7-77.5)	73.0 (64.6-79.4)	73.5 (66.0-80.9)***
Females, %	48.7	46.9	50.5
Comorbidity, median (IQR)[a]	0 (0-1)	0 (0-1)	1 (0-2)
O_2 saturation, median (IQR), %	96 (92-98)	95 (89-98)	92 (85-96)***
Respiratory rate, median (IQR), breaths/min.	24 (20-28)	25 (20-30)	25 (20-30)***
Duration of hospitalisation, median (IQR), days	4.3 (1.9-7.7)	3.8 (1.6-6.8)	3.1 (1.4-5.8)***

IQR = interquartile range.
***) $p < 0.001$ for trend across the 3 periods.
a) By the Charlson Comorbidity Index: 0 = no comorbidity, 1-2 = mild, 3-4 = moderate, ≥ 5 = severe.

The initially measured respiratory rate increased statistically significantly from a median of 24 breaths per minute (BPM) in the first period to 25 BPM in the final period. Oxygen saturation decreased significantly from 96% in the first period to 92% in the last period.

The median duration of hospitalisation decreased significantly from 4.3 days in the first period to 3.1 days in the last period. Duration of hospitalisation was associated with the comorbidity score (tau a = 0.06, $p < 0.001$) and with age (tau a = 0.06, $p < 0.001$).

During the period, 471 patients with COPD died within 30 days of requesting an ambulance (**Table 2**). The 30-day mortality increased from 12.6% in the first to 15.4% in the last period (**Figure 1**). The unadjusted OR of 30-day mortality was higher in the last period (Table 2) than in the first, although this finding was not statistically significant. Adjusting for age and comorbidity lowered the OR of death in the last period compared with the first. Further adjusting for respiratory rate and oxygen saturation lowered point estimates to below 1, but no estimates were statistically significantly different from 1. No statistically significant linear trend was observed in the change of OR for 30-day mortality over the three periods (point estimates 1, 1.1, and 1.3).

TABLE 2 Overview of 30-day mortality among patients with COPD in the North Denmark Region from 2007-2014 and 2016-2018 divided into three periods. Odds ratio for mortality within 30 days is provided with 95% confidence interval and for unadjusted and adjusted logistic regression models in three-time periods with first period as reference.

				OR (95% CI)		
Period	EMS patients with COPD[a], n	Deaths within 30 days, n	30-day mortality, %	unadjusted[b]	adjusted for age, comorbidity[c, d]	adjusted for age, comorbidity, respiratory rate, O_2 saturation[e]
1						
2007	147	12	8.3			
2008	163	21	12.9	1	1	1
2009	167	24	14.4			
2010	237	33	14.0			
2						
2011	213	20	9.4			
2012	305	52	17.2	1.1 (0.8-1.4)	1.0 (0.8-1.4)	0.8 (0.6-1.1)
2013	356	46	13.1			
2014	478	63	13.2			
3						
2016	365	67	18.5			
2017	428	53	12.4	1.3 (1.0-1.7)	1.1 (0.9-1.5)	0.9 (0.6-1.2)
2018	502	80	15.9			

CI = confidence interval; EMS = emergency medical services; OR = odds ratio

a) For patients with > 1 ambulance run, only the last run was included.

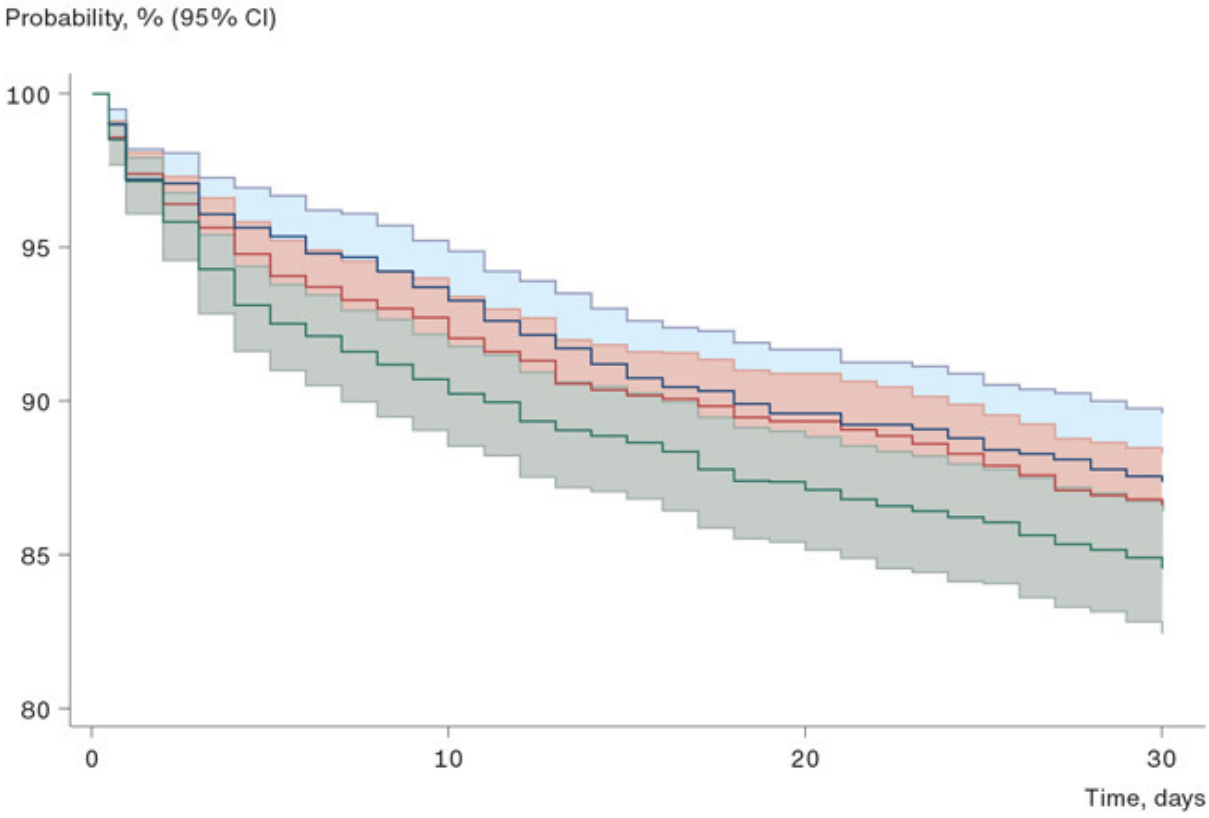
b) p-value for linear trend across the 3 time periods = 0.08.

c) p-value for linear trend across the 3 time periods = 0.3.

d) By the Charlson Comorbidity Index.

e) p-value for linear trend across the 3 time periods = 0.4.

FIGURE 1 Kaplan-Meier plot of observed survival analysis for patients with a COPD diagnosis in the North Denmark Region in the 11-year study period. Cumulative survival probability with 95% confidence interval (CI).



DISCUSSION

The number of patients requesting an ambulance due to COPD doubled in the course of a decade, but this occurred in parallel with an increasing number of ambulance missions. The patients were older in the last period, had more comorbidities and presented with a lower oxygen saturation at the ambulance arrival than the patients of the first period. Despite worsening in the patients' condition, the duration of hospitalisation was reduced in the course of the period.

The observed two-fold increase in the number of ambulance patients with a subsequent COPD diagnosis reflects the increase in the overall EMS activity, as found in a previously study [11].

The increase in acute severity and comorbidity corresponds to those reported in a Danish study of hospitalised patients with COPD in the 2002-2008 period. The use of intensive care increased, inpatient mortality increased from 5.9-7.0% and one-year mortality from 23.2-25.9 [12]. The figures are not directly comparable with our study as the sub-diagnoses included in the COPD definition differ, but the patterns were similar to our findings among the subgroup of COPD patients calling to request an ambulance. We defined COPD according to the main ICD-10 diagnoses to not over-estimate the number of COPD patients in our study.

We cannot compare our results with those published in the Danish Register of Chronic Obstructive Pulmonary Disease annual reports, which show a 30-day mortality of 14% for patients admitted to hospital with acute exacerbation [13]. However, for patients with COPD as the main diagnosis, the 30-day mortality was 12%, while

the subset of COPD patients calling to request an emergency ambulance had a higher mortality, probably also reflecting the severity of the condition.

A comparable Danish study of EMS patients with COPD treated by an anaesthesiologist-manned mobile emergency care unit in the Region of Southern Denmark found a 30-day mortality rate of 10% [3].

Both Danish and international studies found a reduction in the duration of hospitalisation in patients with COPD despite worsening of illness [3, 12, 14]. Compared with the overall reduced duration of hospitalisations from 4.7 in 2008 to 3.7 in 2016 in Denmark, the present study showed an even lower duration of hospitalisation [15].

The OR for 30-day mortality increased in the course of the three periods. When adjusting for age and comorbidity and further for oxygen saturation and respiratory rate, the OR fell, suggesting that the non-significantly higher mortality in the last period compared with the first may be explained by confounding from age, comorbidities and more severe acute illness at ambulance arrival.

One strength of this study was the population-based design, minimising selection bias, another was the linkage of all data sources, facilitating complete follow-up. The use of hospital diagnoses made it possible to identify COPD. The inclusion of hospital diagnoses in the previous five years made adjustment for comorbidities possible, but although the actual COPD diagnosis was not included, previous COPD diagnoses have not been excluded, which may have produced a higher comorbidity score.

We were able to include vital signs registered in the prehospital medical record, allowing us to describe the initial severity of the COPD patient. The initial measurements made at the arrival of the ambulance to the patient's location are of special importance as they reflect the patients' acute condition before initiated treatment. The small difference in respiratory rate may not be of clinical significance; but even so, it does reflect a worsening condition for these patients as a group. The lower initial oxygen saturation, however, clearly indicated a poorer acute condition.

Thus, over the years, COPD patients have become increasingly more acutely ill when calling to request an emergency ambulance, whereas mortality has remained high.

The major weakness of this study was that the total number of deaths was small when analysing trends even though they were divided into only three periods, which may explain the non-significant increase in mortality trend over the years. We had to exclude patients without a civil registration number and were therefore unable to link a COPD diagnosis for all patients. A previous study investigating trends in diagnostic patterns among ambulance patients in the period 2007-2014 found that patients with no identifiable civil registration number constituted 17.8% of all cases [11]. As patients with COPD are chronically ill, they may include fewer patients with missing civil registration numbers, as opposed to accidents or intoxications, affecting the results to a lesser degree. Similarly, the study population only included hospitalised patients, excluding patients treated and released on-scene, and the total number of COPD patients calling for an emergency ambulance may thus have been underestimated in our study.

Finally, defining COPD patients by using the ICD-10 sub-diagnoses may differ between studies. Patients with an underlying COPD diagnosis may be receiving other ICD-10 diagnoses, e.g., J18.9: Pneumonia unspecified or J96: Respiratory failure, not elsewhere classified. A Danish study showed that these diagnoses resulted in an apparent underreporting of COPD among hospitalised patients [16]. We only included COPD as the main diagnosis as we focused on the prehospital setting, and a secondary diagnosis of COPD would not reflect an acute situation.

CONCLUSIONS

The number of patients with COPD admitted to the hospital after calling the emergency number almost doubled from 2007 to 2018. At the end of the study period, patients were older, had more comorbidities and had more severe oxygen saturation and a poorer respiratory rate at ambulance arrival. The nonsignificant trend of increased mortality among EMS patients with COPD was due to patients being older, having more comorbidities and being more acutely ill. Although mortality remained stable, the high level recorded (15%) suggests that COPD patients, who call requesting an ambulance should be considered severely ill.

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